5.4 (old 3.13.4) Follow-up for Hemoglobin Barts (Alpha Thalassemia Major, Hemoglobin H and Hemoglobin H Constant Spring), F Only and FEa

GENERAL INFORMATION: The following hemoglobinopathies are included in this protocol:

"XX" Bart's	Hemoglobin Bart's is ≥90% with no Hb F or A. Consistent with **Alpha Thalassemia Major**, Hydrops Fetalis. In this disorder all 4 alpha globin genes are deleted and most affected infants expire at or soon after birth. Infants who have received intrauterine transfusions or are transfused at birth may survive; a few survivors have successfully received bone marrow transplants.
FAB or FAEB	Hemoglobin Bart's is ≥25% with a characteristic peak on the NBS chromatogram. Consistent with **Hb H Disease** caused by deletion of 3 out of the 4 alpha globin genes, **or Hb H Constant Spring**, a more severe form of hemoglobin H disease in which there are 2 alpha globin gene deletions and an alpha globin gene with the Constant Spring mutation. Persons with Hb H Constant Spring may require transfusions on an occasional or regular basis. Parents need to be instructed about certain oxidizing substances that could cause severe anemia in children with Hb H Disease. Hb H disease can occur along with Hb E trait, or, rarely, with some other beta globin trait.
F only	Consistent with **Beta thalassemia Major**, a severe, transfusion-dependent hemoglobinopathy.
FEa	Consistent with **Hb E beta^{+} thalassemia**, which may cause serious anemia and possibly require transfusions.

POLICY: Written notification to parents and physicians will be made utilizing state-approved Parent and Doctor Letters (See Sections 11.1 & 11.2).

Attachment:

5.1.2 California NBS Program Recommendations for Care of Infants with Newborn Screening Results of Thalassemia Disease

5.4 Follow-up for Hemoglobin Barts (Alpha Thalassemia Major, Hb H and Hb H Constant Spring), F Only and FEa

PROTOCOL:

RESP. PERSON	ACTION
ASC NBS Coord/Program Specialist	• **Daily** reviews the Headline Case Report for significant non-sickling hemoglobinopathy cases • **Within 48 hrs. of obtaining positive result** notifies the physician of record by phone of the screening result and requests blood specimens to be drawn from the infant and both parents for confirmatory testing as soon as possible to rule out a significant hemoglobin disorder. If the baby has expired, as often occurs in Alpha Thalassemia Major, the ASC can assist the PCP by coordinating follow-up parent testing (free of charge for specimens sent to the Hemoglobin Reference Lab) and genetic counseling at a CCS Sickle Cell Disease Center. • Assists primary care provider (PCP) with referral to a CCS Sickle Cell Disease Center (SCDC) (see 7.2 *Referral to CCS Special Care Centers*). Because current testing methodology for identifying infants with thalassemia diseases has a high level of specificity, infants with positive screening results should be referred to a CCS Sickle Cell Disease Special Care Center (SCDC) for follow-up care and parent teaching without waiting for the results of confirmatory testing. • Sends appropriate **Doctor Letter depending on diagnosis** to physician, summarizing the phone call along with a copy of the *California NBS Program Recommendations for Care of Infants With Newborn Screening Results of Thalassemia Disease* (5.1.2). • Sends *Instructions for Collection, Handling, and Mailing of Blood Specimens for Confirmatory Testing* (5.8) as well as the mailing materials (cylinder, GSO label) to lab obtaining the confirmatory specimen. • For Hb H enclose "*Fact Sheet on Alpha Thalassemia*" *and "Why Does My Baby Need More Testing for Alpha Thalassemia*". **NOTE: there are no "Why Retest" pamphlets for Hb Bart's Only (Alpha thalassemia Major), Hb F Only or Hb FEa**; the brochure entitiled "*Why Retest for Hemoglobin E/beta thalassemia"* is only for NBS results of Hb FE. • **Within 2-3 days**, follows up with the PCP to find out if family has been contacted. • **After confirming that family has been notified**, calls family and reinforces information given by physician and sends appropriate **Parent Letter depending on diagnosis**. **For Hb H**, sends brochure, "*Why Retest for Alpha Thalassemia*" with parent letter.

	• Continues to attempt parent contact if initially unsuccessful. • If asked by the PCP to notify the family directly, after the contact is made, sends **Parent Letter depending on diagnosis** confirming discussion with the parent and providing information about immediate follow-up care for the infant. **For Hb H**, includes the brochure "*Why Does My Baby Need More Testing for Alpha Thalassemia*". • Makes referral to CCS (See 7.2 *Referrals to CCS Special Care Centers*). • **After one week of the physician and/or Coordinator trying to contact the family**, sends **Parent Letter #2** by regular and certified mail with receipt requested informing the family to call the newborn's PCP or Coordinator regarding baby's test results. • **If contact with the family is still not made one week after sending Parent Letter #2**, makes arrangements for home visit by local health department public health nurse.
Hb Reference Lab	• Conducts confirmatory testing on liquid blood specimen(s). • **Within 11 working days** enters results in SIS and informs the ASC NBS Coordinator of the confirmatory test results by fax or phone, followed by a hard copy sent to the ASC NBS Coordinator and NBSB Hemoglobin Coordinator. Includes the following results: A) Separation of hemoglobins F, A, S, C, D, and E with relative concentrations for each hemoglobin on all specimens by cellulose acetate-citrate agar electrophoresis, isoelectric focusing, high pressure liquid chromatography, and/or DNA analysis as outlined in the Hb Reference Lab NBS vendor agreement scope of work or as approved by the NBSB.. B) Hemogram on each suitable specimen, to include hemoglobin, hematocrit, and mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH). C) Free Erythrocyte Protoporphyrin (FEP) on specimens with microcytic hypochromic anemia. D) Quantitative Hb A2 when necessary to resolve phenotype. E) Quantitative Hb F when necessary to resolve phenotype. • **Within 31 calendar days of receipt of specimen(s)**, enters results in SIS, faxes and mails reports on: a. Beta globin DNA analysis: • to determine the beta thalassemia mutations in E/ Beta^0 or E/Beta$^+$ Thalassemia and Beta Thalassemia Major • to examine inconsistencies between thin layer isoelectric focusing profiles of newborn and parents. b. DNA analysis for alpha globin deletions and other point mutations on samples with significant amounts of Hb Barts.

	c. Presumptive findings for unusual Hb variants such as Hb Korle Bu, Hb T Cambodian, Hb Matsue-Oki, Hb O Arab, Hb C Harlem, Hb G Philadelphia. • **Within 91 calendar days of receipt of specimen(s)** enters results in SIS, faxes and mails reports on analysis of rare variants carried in compound heterozygosity with clinically significant hemoglobins.
ASC NBS Coord./ Program Specialist	• **Phones the NBS Hb Coordinator with any confirmatory results that are inconsistent with the NBS results prior to contacting the PCP.** Confirmatory results showing alpha thalassemia trait (2-gene deletion) require investigation of anomalous results by the NBS Hb Coordinator. In these cases follow-up may be recommended by a Consulting Hematologist depending on the initial Bart's % and clinical symptoms. • Phones the PCP with the confirmatory test results. • **Sends appropriate follow-up Doctor Letter depending on diagnosis** with the lab report to the PCP and includes a copy of the *Diagnosis And Treatment* form to be used for reporting the disease. For confirmatory results indicating Hb H Disease or Hb H Constant Spring Disease, includes a copy of the "*Parents Guide to Hemoglobin H Disease*". • Sends a copy to the CCS Sickle Cell Disease Center (SCDC) following the infant. • Resolves case in SIS when *Diagnosis & Treatment* form has been received, or the SCDC has completed the Hemoglobin Service Report in SIS indicating that infant has been seen and treatment is either initiated or not required. See Case Resolution Protocol 7.30. • Reports any missed cases to NBS Hb coordinator, and lost to follow-up cases or other unusual occurrences of potential significance to NBSB Nurse Consultant/ASC Contract Liaison. • Refers case to Child Protective Services (CPS) as appropriate and with approval of NBS Nurse Consultant/Contract Liaison *(See 7.1 Referral of Cases to Child Protective Services)*